II. Non-Technical Abstract

There are presently more than 40,000 new cases of melanoma in the U.S. per year with 7,300 melanoma-related deaths. Patients with stage III disease have at least a 50% chance of recurrence after surgical resection; patients with stage IV melanoma have a median survival of less than 1 year and most of these patients eventually die of melanoma. Standard therapy is dacarbazine chemotherapy, and while response rates range from 8-25%, there is little evidence that treatment improves survival. Combination chemotherapy and biochemotherapy regimens have been reported to induce higher response rates with the disadvantage of greater toxicity and, to date, there is no evidence that they result in improved survival. New approaches to the treatment of this disease are needed.

The overall goal of this study is to develop ways to vaccinate against melanoma. In particular, we are trying to immunize against two proteins found in melanoma cells that help to produce its black color, tyrosinase and gp100. To do this, we will inject a small piece of each of these proteins. These small pieces are called peptides. We know that these peptides alone won't be enough to stimulate the immune system. We will first have to inject something called an adjuvant that will further stimulate the immune system. In this study, we plan to use granulocyte-macrophage colony-stimulating factor (GM-CSF) DNA as an adjuvant. This study is designed to establish a safe and effective dose of GM-CSF DNA. The adjuvant is a piece of DNA purified from bacteria, which contains the gene for GM-CSF. DNA is the blueprint that cells use to produce the substances that make up the body. GM-CSF is produced by many cells of the body. It stimulates different parts of the immune system. The vaccine will be produced at Memorial Sloan-Kettering Cancer Center. The gene was obtained from immune cells from a healthy donor. We use bacteria to produce the DNA that will be used for this vaccine. We will also see if the adjuvant causes any side effects. All of the patients on this study will receive vaccine. Because we do not know what the best dose of GM-CSF DNA is, groups of patients in the first part of the study will receive increasing doses of GM-CSF DNA with the peptides. The first patients to be treated will receive lower doses than the later patients. We will watch each group for side effects before we move on to a higher dose. After we find the highest dose we can give, patients treated in the second part of the study will receive that dose. We expect 18 patients to participate in this study.

Patients will be treated in the outpatient Clinical Immunology unit and will receive 3 monthly vaccinations into the skin. They will receive GM-CSF DNA delivered intradermally, followed by administration of both peptides to the same site on day 5. The GM-CSF DNA injections are given intradermally by a needleless device called a Biojector2000. This device is held in the hand and shoots the vaccine into the muscle. Blood will be drawn at regular intervals for analysis of T-cells. We will also be monitoring patients for any evidence of an effect on tumors.